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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,296	06/23/2006	Heinrich Haas	062587-5011	4615

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EXAMINER	
PURDY, KYLE A	

ART UNIT	PAPER NUMBER
1611	

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09/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,296	HAAS ET AL.	
	Examiner	Art Unit	
	Kyle Purdy	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/04/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 23-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *0.32,1-15 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet (08/13/2008)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the amendments filed on 06/04/2008 wherein claims 1, 3, 6, 11-13 have been amended, claims 16-22 have been cancelled and claims 23-32 have been newly added.

2. Claims 1-15 and 23-32 are presented for examination on the merits. The following rejections are made.

3. Note, claim 14 is currently listed as 'currently amended'; however no amendment has been made to the claim.

Response to Applicants' Arguments

4. Applicants arguments filed 06/04/2008 regarding the rejection of claims 1-15 made by the Examiner under 35 USC 112, second paragraph have been fully considered and they are found persuasive. This rejection is withdrawn as being overcome by amendment.

5. Applicants arguments filed 06/04/2008 regarding the rejection of claims 1, 8-11 and 15 made by the Examiner under 35 USC 102(b) as being anticipated by Huang et al. (US 6008202) have been fully considered but they are found persuasive. This rejection is withdrawn as being overcome by amendment.

6. Applicants arguments filed 06/04/2008 regarding the rejection of claims 1-15 made by the Examiner under 35 USC 103(a) over Slater et al. (US 6355268) in view of Cullis et al. (Biochemica at Biophysica Acta, 1997, 1331, 187-211) have been fully considered but they are found persuasive. This rejection is withdrawn as being overcome by amendment.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. **Claims 1 and 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Burke (US 5552156).**

9. Burke is directed to liposomal and micellar stabilization of camptothecin drugs. Methods for making camptothecin loaded micelles are disclosed (see Examples 3 and 10). Example 3 teaches mixing preformed cationic micelles in a suspension with camptothecin and giving the mixture time to equilibrate to form drug loaded micelles (see instant claims 1, 8 and 9). The micelles of Example 3 are made from dimyristoyl phosphatidylcholine (DMPC) is a cationic lipid and is amphipihlic (see isntant claims 10 and 11). It is noted that the mixture of Example 3 is aqueous (see instant claim 1). It is disclosed that camptothecin drugs bind the lipid bilayer membrane of the liposome and so it must be partially able to penetrate said membrane (see column 2, lines 10-15; see instant claim 1).

10. Thus, Burke anticipates the instantly rejected claims.

11. **Claims 1, 2, 4, 5, 7-11, 15 and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Munich Biotech (EP 1393719; of record, see IDS).**

12. Munich is directed to camptothecin carboylate formulations. A method of making such formulations is disclosed on page 11, Organic Solution Injection. Liposomal suspension can be achieved through injection of a solution of lipid (in ethanol) into an aqueous solution containing carboxylate camptothecin (see instant claims 1, 4, 5 and 7). The liposome comprises cationic lipids such as DOTAP (see page 11; see instant claims 9-11 and 30). It is taught that the carboxylic camptothecin is amphiphilic (see page 3). Therefore, it would be capable of partially penetrating into a membrane (see instant claim 1). The pH of the suspension may be from 5 and 9, however in the Examples, a pH of 7.5 is utilized (see page 11; see instant claim 15).

13. Thus, Munich anticipates the instantly rejected claims.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. **Claims 3, 6, 12-14, 16-29, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Munich Biotech (EP 1393719; of record, see IDS).**

16. Munich is relied upon for disclosure described in the rejection of claims 1, 2, 4, 5, 7-11, 15 and 30 under 35 U.S.C. 102(a).

17. It is noted that Munich is directed to compositions that are substantially free from the lactone form of camptothecin (see abstract). It is taught that the drug is present from between 5 to 15 mol% with respect to the cationic colloidal nanoaggregate (i.e. cationic nanoparticle) (see

page 5; see instant claims 3 and 23-25). It is also taught that the cationic amphiphile can be a polyvalent (i.e. a cationic polyelectrolyte) (see page 4; see instant claim 29). Moreover, it appears that the compositions are suitable for administration after mixing adnd loading of the micelles (see pages 14 and 15; see instant claims 14) wherein the compositions are administered to mice and humans.

18. Muich fails to teach a specific mixing time (i.e. about 2 hours) and temperature (i.e. about 25°C. Munich also fails to specifically teach the proportion of the carboxylate to the lactone camptothecin form.

19. Regardless, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teaching of Munich with a reasonable expectation for success in arriving at a method of making carboxylate-camptothecin loaded nanoparticles wherein the nanoparticles comprise cationic lipids. It is acknowledged that Munich fails to specifically teach a mixing time for the lipid micelles and drug, but this parameter is obvious. One of ordinary skill in the art would endeavor to optimize this parameter because the length of time required to load the nanoparticle would be directly related to the amount of drug loaded. With respect to the temperature of the mixing step, such a parameter would be obvious. In the instant case, no specific temperature is disclosed for their mixing step. As such, it would be reasonable to assume that the process was carried out at room temperature (i.e. 25°C). Finally, with respect to a specific percentage of lactone to carboxylic camptothecin, this is also obvious. Although Munich fails to specifically teach a ratio of one to the other, Munich does state that the compositions are to be substantially free of the lactone form. It is the position of the Examiner that 'substantially free of' would suggest to one of ordinary skill a percentage less than at least 1

or 2%, and preferably none at all. Therefore, a method of loading nanoparticles with carboxylic camptothecin is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

Conclusion

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

21. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

23. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

24. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kyle Purdy/
Examiner, Art Unit 1611
August 27, 2008

/Sharmila Gollamudi Landau/
Supervisory Patent Examiner, Art Unit 1611